REMARKS/ARGUMENTS

Reconsideration of this application is requested. Claims 78-80 are under consideration. Claims 1-77 and 81-127 are withdrawn from consideration.

I. INFORMATION DISCLOSURE STATEMENT

Legible copies of documents indicated as not considered by the Examiner in the attachments to the outstanding Official Action are attached to the present response, together with a completed PTO-1449. Consideration and entry of the attached references are respectfully requested.

II. THE 35 U.S.C. §112, SECOND PARAGRAPH, REJECTION

Claims 78-80 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite for the reasons stated on page 2 of the Action. In response, claim 78 has been amended to delete both occurrences of "test". Claim 78 has been rejected on the grounds that "preferentially" "is a term of degree which renders the scope of the claim indefinite." (Office Action, page 2). The Office is quite correct that "preferentially" is a term of degree, but that is no defect as long as the "patent's specification provides some standard for measuring that degree." *Seattle Box Co., Inc. v. Industrial Crating & Packing, Inc.,* 731 F.2d 818, 826; 221 U.S.P.Q. (BNA) 568, 574 (Fed. Cir. 1984). Applicants' claimed invention is directed to a comparative method in which the standard for measuring the degree of preferential killing is at the heart of the invention. In accordance with the invention of claim 78 a comparison is made of the relative ability of a virus to kill cells that are either deficient or competent in an interferon-mediated viral

activity. If the virus preferentially kills the deficient cells as compared to the competent cells, then the virus is identified as having antineoplastic activity. The words "as compared to" have been inserted into claim 78 after "preferentially" to emphasize and further clarify the comparative nature of the claimed method.

Withdrawal of the outstanding 35 U.S.C. §112, second paragraph, rejection is now believed to be in order. Such action is respectfully requested.

III. THE OBVIOUSNESS REJECTION

Claim "1" (it is believed that the Examiner intended to refer to claim 78) stands rejected under 35 U.S.C. §103(a) as allegedly unpatentable over U.S. Patent 5,677,178 to McCormick in view of Stiehm et al. (hereinafter Stiehm). That rejection is respectfully traversed.

Claim 78 is directed to a method for identifying a virus with antineoplastic activity in a mammal. The method comprises using the virus to infect cells deficient in an interferon-mediated antiviral activity and cells competent in an interferon-mediated antiviral activity and determining whether the virus kills the cells deficient in an interferon-mediated antiviral activity preferentially as compared to the cells competent in interferon-mediated antiviral activity.

The Examiner admits that McCormick does not teach infecting cells that are deficient in an interferon-mediated antiviral activity. In an attempt to cure this deficiency, the Examiner relies on Stiehm, and asserts that Stiehm discloses that interferons produce an antiviral state in uninfected cells by altering the nucleotide metabolism and cytoplasmic enzyme induction of non-infected cells (citing to lines 1-3).

The Examiner asserts that, at the time of the present invention, one of ordinary skill would have been motivated to combine the disclosures of McCormick and Stiehm, first because infecting cells having varying interferon-mediated activity would permit the method of McCormick to identify a different class of anti-neoplastic viruses and, second, because McCormick's disclosure expressly suggests the asserted combination.

In response, prior to the present invention, it was not known to those of ordinary skill in the art that tumor cells were generally defective in interferon responsiveness. Indeed, Stiehm teaches (see: p 90, "Non-Hodgkin's Lymphoma") that tumor cells are responsive to the effects of interferon, as evidenced by the occurrence of clinical responses following interferon treatment. Thus, based on McCormick and Stiehm the person of ordinary skill in the art would not have had a reasonable expectation that viruses that preferentially kill cells deficient in an interferon-mediated antiviral activity would have antineoplastic activity. To the contrary, based on Stiehm, it would have been just as reasonable to expect that differential killing of cells deficient or competent in an interferon-mediated antiviral activity would not be correlated with antineoplastic activity.

It is important to note that decreased interferon production, including from *normal* leukocytes in lymphoma patients, as indicated by Stiehm, does not equate to and cannot be interpreted as tumor cell defects in the response to interferon, or in regard to defects in antiviral activity in *tumor* cells. Therefore, it does not follow that one of ordinary skill in the art would have been motivated to combine the teachings of McCormick and Stiehm.

The Examiner contends McCormick "expressly suggests the asserted combination" (with Stiehm) when it states the method of ablating neoplastic cells is "applicable to essentially *any virus* wherein efficient replication requires binding and/or sequestration and/or *inactivation of a host cell protein* that is present in non-neoplastic cells but is substantially absent or non-functional in neoplastic cells". This contention is wrong for at least three reasons.

First, Stiehm does not disclose viral replication as a consequence of the inactivation of a host cell protein. Second, as disclosed by McCormick, p53 is a tumor suppressor gene (see: column 1, line 29) and is not understood to encode for an antiviral protein such as interferon. McCormick discloses that the ability of p53 to affect viral replication is limited to adenovirus and papovaviruses. Therefore, the combination with Stiehm, which discloses interferon as possessing broad antiviral activity, would **not** have been obvious to one of ordinary skill. Third, neither McCormick nor Stiehm discloses which host cell protein(s) involved in interferon-mediated activity must be bound, sequestered, or inactivated by a viral protein for efficient replication. Nor do they disclose or suggest which viral proteins of which viruses are targets for recombination to ablate said binding, sequestration or inactivation of the unidentified host cell protein.

Based on the above, it is clear that one of ordinary skill would **not** have been motivated to combine the disclosures relied on by the Examiner. Moreover the theoretical combination of the references would not have suggested the claimed invention. Absent any such motivation, a *prima facie* case of obviousness has not been generated in this case. Reconsideration and withdrawal of the outstanding obviousness rejection are accordingly respectfully requested.

Favorable action on this application is awaited.

Respectfully submitted,

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